

Applicants: Richard Deckelbaum et al.  
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**REMARKS**

Claims 1-3, 10-11, 15-17, and 24-25 are currently pending under examination, and claims 12-14, 18-23, and 26-30 are withdrawn from consideration. Applicants have hereinabove canceled claims 2, 10-14, 18-23, and 25-30 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future application. In addition, applicants have hereinabove amended claims 1, 3, 15, and 24. Support for the amendments to claim 1 can be found in the specification as originally filed at, *inter alia*, page 14, line 26 to page 15, line 3; and page 22, lines 11-15. Claim 3 has been amended merely to correct dependency. Support for the amendments to claim 15 can be found in the specification as originally filed at, *inter alia*, page 22, lines 20-34; and page 22, lines 11-15. Support for the amendments to claim 24 can be found in the specification as originally filed at, *inter alia*, page 24, lines 19-29; and page 22, lines 11-15. Applicants maintain that the amendments to the claims raise no issue of new matter. Accordingly, applicants respectfully request entry of this Amendment. After entry of this Amendment, claims 1,3,15-17, and 24 will be pending and under examination.

**Claims Rejected Under 35 U.S.C. §102(b)**

In the November 28, 2003 Office Action the Examiner stated that claims 1-3, 11, and 24-25 are anticipated under 35 U.S.C. §102(b) by Treskova et al. The Examiner further stated that applicants claim an emulsion consisting of a pharmaceutical agent, fish oil and emulsifier. The Examiner stated that the fish oil is an omega 3 triglyceride; the composition is delivered to extrahepatic tissue; the omega 3 triglyceride

effects delivery of the pharmaceutical agent; and the composition has 80% of the particles with a diameter of 150-350 nm. The Examiner further stated that applicants additionally claim an emulsion consisting of a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride. The Examiner also stated that Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). The Examiner stated that Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (Abstract). The Examiner stated that the reference anticipates the claimed subject matter.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have hereinabove amended claims 1 and 24. Applicants note that Treskova et al. do not teach all the elements of applicants' claimed invention in that they do not teach a composition wherein more than 80% of the particles have a diameter of between 30 and 150nm, as recited in of claims 1, 15, and 24. Accordingly, Treskova et al. does not anticipate the claimed subject matter, and applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

**Claims Rejected Under 35 U.S.C. §103(a)**

The Examiner stated that claims 1-3, 10-11 and 24-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over

Pscherer, Wretlind or Boll. The Examiner stated that Pscherer teaches lipid emulsions comprising MCT, LCT, omega 3 triglycerides in the form of fish oil, emulsifiers and vitamin E (a pharmaceutical agent) (col.2 - 4). The Examiner stated that the particle sizes are less than 0.5 micrometers (col.5, line 6-7).

In response, applicants respectfully traverse the Examiner's rejection. Applicants maintain that the Pscherer et al. do not teach all the elements of applicants claimed invention. Specifically, with regard to claim 1, applicants note that Pscherer et al., as indicated by the Examiner in the November 28, 2003 Office Action, teach emulsions that contain either LCTs, or MCTs, or both, and further note that applicants' claimed invention recites neither LCTs or MCTs. Moreover, applicants note that there is no teaching in Pscherer as to why LCTs or MCTs would be omitted from the emulsions discussed. With regard to claim 24, applicants note that, as the Examiner states, Pscherer et al. teach an emulsion which contains fish oil. In contrast, claim 24 does not recite such a component. Moreover, applicants note that there is no teaching in Pscherer as to why fish oil would be omitted from the emulsions discussed. Accordingly, applicants maintain that the rejected claims are not properly rejected under 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that Wretlind et al. teach emulsion compositions for delivering therapeutics (Abstract), the composition comprising fish oil (which intrinsically contains omega 3 triglycerides), emulsifiers, pharmaceutical agents and LCT with particle sizes of 0.005 - 0.5 microns (5 - 500 nm) (col.4).

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In response, applicants respectfully traverse the Examiner's rejection. Specifically, with regard to claim 1, applicants note that Wretlind et al., as indicated by the Examiner in the November 28, 2003 Office Action, teach emulsions that contain both fish oil and LCTs. Applicants claimed invention does not recite LCTs, nor is there any teaching in the cited reference as to why LCTs would be omitted from the emulsions. With regard to claim 24, applicants note that, as the Examiner states, Wretlind et al. teaches an emulsion which contains fish oil. In contrast, applicants' claimed invention does not recite such a component. Accordingly, applicants maintain that the rejected claims are not properly rejected under 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that Boll et al. teach lipid emulsions containing omega 3 fatty acids as fish oil, an emulsifier, MCT and tocopherols (a pharmaceutical agent) for endotracheal treatment (Abstract).

In response, applicants respectfully traverse the Examiner's rejection. Specifically, with regard to claim 1, applicants note that Boll et al., as indicated by the Examiner in the November 28, 2003 Office Action, teach emulsions that contain both fish oil and MCTs. Applicants claimed invention does not recite MCTs, and further note that there is no teaching in the reference as to why MCTs would be omitted from the emulsions taught in Boll. With regard to claim 24, applicants note that, as the Examiner states, Boll et al. teaches an emulsion which contains fish oil. In contrast, applicants' claimed invention does not recite such a component. Accordingly, applicants maintain that the rejected claims are not properly rejected under 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

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The Examiner additionally stated that, although the references do not teach the component amounts are predetermined to delivery pharmaceutical agents to predetermined tissues, such activity is intrinsic to the pharmaceutical compositions. The Examiner stated that, in addition, the references do not teach the claimed particle sizes. The Examiner stated that, however, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such parameters as a matter of routine experimentation. The Examiner stated that moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of the reference compositions with a reasonable expectation for successfully obtaining effective pharmaceutical compositions. The Examiner stated that while the references teach the compositions to include additional components, it would have been well within the purview of one of ordinary skill in the art to omit components where their functions are not desired. The Examiner stated that applicants argue that the references contain additional ingredients and therefore do not anticipate the claims. The Examiner stated that however, this argument fails to persuade because while the reference compositions may contain additives for preservation, flavor or other functions, it would certainly have been obvious to one of ordinary skill in the art to omit such components where such functions are not desired or required. The Examiner stated that therefore, the claims are rejected for these reasons, and those made above.

In response, applicants note that the Examiner has not stated what the non-desired functions are with respect to MCTs and/or LCTs, and therefore has not stated where the motivation to omit MCTs and/or LCTs comes from, i.e. why such functions

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would not be "desired or required". Applicants maintain that impermissible hindsight is being employed in this instance, and that no support is found in the references cited for omitting MCTs from the emulsions taught by Boll, LCTs from the emulsions taught by Wretlind et al., or MCTs and/or LCTs from the emulsions taught by Pscherer et al. Accordingly, applicants maintain that the rejected claims are not properly rejected under 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-3, 10-11 and 24-25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Treskova et al. The Examiner further stated that Treskova et al. teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). The Examiner also stated that Treskova et al. teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract). The Examiner stated that although Treskova et al. does not teach the emulsions with particle sizes of 30-150 nm, it would have been well within the purview of one of ordinary skill in the art to optimize particle size as a matter of routine experimentation (see other cited references for support). The Examiner stated that therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of Treskova et al. with a reasonable expectation for successfully obtaining an effective emulsion composition. The Examiner stated that as such, the claims stand rejected as being anticipated by Treskova et al.

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In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have hereinabove amended claims 1 and 24. Applicants note that Treskova et al. does not teach all the elements of applicants' claimed invention in that it does not teach the particle size of 30-150nm recited in the claims, and moreover, does not recite the characteristic that more than 80% of the particles are of this size. Applicants further note that there is no motivation in the cited references to obtain an emulsion of these characteristics. In response to the Examiner's position that particle size would have been optimized as a matter of routine experimentation, applicants note that what is optimal depends on the intended function of the product, and there is no teaching in the cited references that 80% of particles of 30-150nm is the optimal size, and in fact other particle sizes are taught, e.g. Counsell teaches 50-200nm, Wretlind teaches 50-500nm, Pscherer teaches up to 500nm. Moreover, the disclosure of particle size effecting preferential tissue delivery, as shown by applicants e.g. see Figure 8, is not taught in the cited articles. Accordingly, Treskova et al. does not make obvious the claimed subject matter, and applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1, 3, 10-11, 15-17 and 24-25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Treskova et al. and Counsell et al. The Examiner stated that Treskova et al. teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form offish oil, with emulsion particle sizes of about 300 nm (p.254). The Examiner stated that Treskova et al.

teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract). The Examiner also stated that Counsell et al. teaches emulsions for hepatic tissue selective delivery of Pharmaceuticals (abstract), comprising a lipophilic core and emulsifier (col. 5 line 50-59). The Examiner stated that the core may contain LCT and fish oils (col. 5 line 66 - col. 6 line 9, col.1 1), and the emulsion particle size is 50-200 nm (abstract). The Examiner further stated that the above references do not specifically teach the emulsions comprising the ligand apolipoprotein E, or homologs thereof. The Examiner stated that however, Treskova et al. does suggest that uptake of the triglycerides is increased in the presence of apolipoprotein E (p.257). The Examiner stated that in addition, Counsell et al. teaches that the emulsion must associate with apolipoprotein E to make it hepatocyte specific (col. 4-5). The Examiner also stated that at the time of the claimed invention, one of ordinary skill in the art would certainly have been motivated by the teachings of Treskova and Counsell to include apolipoprotein E, or homologs thereof, in the disclosed compositions for it's specificity to hepatic and extrahepatic tissues, and for the disclosed effect of increasing triglyceride uptake. The Examiner stated that moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Treskova and Counsell to include apolipoprotein E or homologs thereof in the compositions with a reasonable expectation for successfully obtaining an emulsion for delivering an agent to extrahepatic tissue. The Examiner stated that therefore, for these reasons and those above, the claims remain rejected.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that Counsell et al. teach away from combining it with the teachings of Treskova et al. in



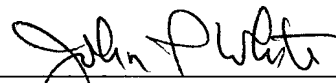
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that Counsell et al. teach emulsions containing cholesterol (see Abstract) and, moreover, states at Col. 5, line 22, that the composition "must contain a sterol", whereas Treskova et al. teach emulsions not containing sterols, see Abstract for example. In light of these teachings, there is no motivation to combine the cited references and the claims are not properly rejected under 35 U.S.C. §103. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

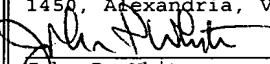
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450	
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